Poster III-60

Novel Approaches in Computer Simulation of Infections: Sim2Virus and PathSim as Prototypes

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We are engaged in a simulation and modeling program to better understand the various strategies that pathogens, especially viral pathogens, employ to cause clinical disease. We employ three different approaches to simulating virus-host interactions. Two are agent-based, with an initial set of three agent types, *e.g.,* epithelial and immune cells and viruses, interacting according to specified rules, and the third employs ordinary differential equations. One of our prototype viruses is murine hepatitis virus (MHV), a member of the coronavirus family that causes a demyelinating disease in mice clinically similar to the human disease, multiple sclerosis. The second virus is Epstein-Barr Virus (EBV), a ubiquitous and sometimes pathogenic human herpes virus that establishes a life-long persistent infection in B lymphocytes despite an aggressive immune response.

The first simulation, Sim2Virus, is a simple stochastic simulation developed to examine spatial spread and partitioning of two viruses *in vitro*. It is currently being expanded to incorporate cellular and viral biochemistry. We will also discuss a modified version that allows for a mathematical specification of the computer model as a discrete dynamical system. This makes available more sophisticated mathematical analysis tools. The EBV model, PathSim, is more sophisticated. The tonsillar ring is represented as a virtual world linked to a Web-based graphical user interface. Not only is direct visualization of simulated events possible, but rigorous analysis of output, through a suite of information visualization tools. We are developing a mathematical specification for the simulation that enables the identification of factors responsible for specific dynamic trajectories. Moreover, desired outcomes, *e.g.,* complete viral clearance following the acute phase, can potentially be reverse-engineered. The third model, employing ordinary differential equations, is based on standard population dynamics for viral infections and clearance. Our first prototypes represent models that will eventually be applicable to a wide range of host-pathogen systems. The long-range goal is the generation of predictions that can be experimentally tested such that *in silico* simulation can substitute for human and/or animal experimentation. Parallel animal and human disease course simulations would allow comparisons and further our understanding of similarities.